

## REMARKS

In the Office Action of March 29, 2004, the Examiner rejected claims 66 -110 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully disagree with this rejection.

As explained below, applicants were fully in possession of the invention claimed in claims 66 –110 and also provided enabling disclosure for these claims. The Examiner seemed to acknowledge that the subject matter of these claims is disclosed in this application (and were disclosed in the parent US Application 09/005,985). Indeed, these claim elements were not only disclosed but also claimed (however, not claimed in combination with the claimed low volume hybridization device).

Specifically, the subject matter of claims 66 – 70 was claimed in the original claim 50, the subject matter of claims 71 and 72 was claimed in the original claim 1, the subject matter of claim 73 was claimed in the original claim 5, the subject matter of claim 75 was claimed in the original claim 6, the subject matter of claims 76, 77, and 79 - 86 was claimed in the original claims 10 – 12 and 16 – 21, respectively. The similar applies to claim 96 – 110.

Therefore, Applicants believe that the Examiner had a question regarding the combination of the claim elements recited in claims 66 – 110 and the low volume hybridization device (specifically described in col. 51 line 38 through col. 52 line 45 of the parent US Pat. 6,168,948). However, the present specification made it clear that although described in terms of individual devices, the present specification is directed to the combination of the described devices. On page 9 line 26, the present specification states:

It is a general object of the present invention to provide a miniaturized integrated nucleic acid diagnostic devices and systems incorporating these devices. The devices of the invention are generally capable of performing one or more sample acquisition and preparation operations, as may be integrated with one or more sample analysis operations. For example, the devices can integrate several or all of the operations involved in sample acquisition and storage, sample preparation and sample analysis, within a single, miniaturized, integrated unit. The devices are useful in a variety of applications and most notably, nucleic acid based diagnostic applications and de novo sequencing applications.

The devices of the invention will typically be one component of a larger

diagnostic system, which further includes reader device for scanning and obtaining the data from the device, and a computer based interface for controlling the device and/or interpretation of the data derived from the device.

To carry out their primary functions, one embodiment of the devices of the invention will typically incorporate a plurality of distinct reaction chambers for carrying out the sample acquisition, preparation and analysis operations. In particular, a sample to be analyzed is introduced into the device whereupon it will be delivered to one of these distinct reaction chambers which are designed for carrying out a variety of reactions as a prelude to analysis of the sample. These preparative reactions generally include, e.g., sample extraction, PCR amplification, nucleic acid fragmentation and labeling, extension reactions, transcription reactions and the like.

Furthermore, on page 117, line 16, the present specification states:

Although generally described in terms of individual devices, it will be appreciated that multiple devices may be provided in parallel to perform analyses on a large number of individual samples. Because the devices are miniaturized, reagent and/or space requirements are substantially reduced. Similarly, the small size allows automation of sample introduction process using, e.g., robot samplers and the like.

Importantly, the subject matter of claim 66 - 110 was described and claimed in one document together the low volume hybridization device specifically described in col. 51, line 38 through col. 52 line 45 of the parent US Pat. 6,168,948 (mentioned by the Examiner). Surely, a person of ordinary skill in the art would be able to combine the device elements described in one document. After all, in the obviousness rejections, the Examiner combined two or three separate and distinct references and asserted that the person of ordinary skill in the art would be able to combine these separate references. Therefore, the original specification (including the original claims) reasonably conveys to one skilled in the relevant art that the inventors, at the time the priority application was filed, had possession of the invention claimed in claims 66 - 110.

The Examiner rejected claims 74 and 99 under 35 U.S.C. §112, second paragraph, as being indefinite. Applicants amended these claims to overcome this rejection.

The Examiner also rejected claims 45-48, 71, 78-96 and 102-110 under 35 U.S.C. §103(a) as being unpatentable over US Pat. 5,882,903 to Andrevski et al. in view of US Pat. 5,863,502 to Southgate et al. The Examiner also rejected claims 72, 73, 75-77, 79, 97, 98, 100, 101 and 103 under 35 U.S.C. §103(a) as being unpatentable over US Pat. 5,882,903 to Andrevski et al. in view of US Pat. 5,863,502 to Southgate et al. taken further in view of US Pat. 5,876,918 to Wainwright et al. The Examiner also rejected claims 78, 80-86, 102 and 104-110 are rejected under 35 U.S.C. §103(a) as being unpatentable over US Pat. 5,882,903 to Andrevski et al. in view of US Pat. 5,863,502 to Southgate et al. taken further in view of US Pat. 5,229,297 to Schnipelsky et al. Applicants respectfully disagree with the above rejections if again applied to the amended claims.

As separately recited in independent claims 45 and 91 the claimed invention is a low-volume hybridization device that includes a base, a pressure chamber, and a reaction chamber including a probe array for hybridization. According to the novel concept used for small volumes, the reaction chamber is bound by a flexible diaphragm separating the pressure chamber from the reaction chamber. By applying pressure or vacuum via the pressure chamber, the flexible diaphragm enables mixing of the fluid in the reaction chamber and thus facilitates the hybridization over the area of the probe array.

The claimed invention differs patentably from the cited prior art. While US Pat. 5,882,903 to Andrevski et al. (i.e., the primary reference) discloses a small volume reaction chamber 250 (or chambers 250A – 250C), the Andrevski design is not suitable for hybridization over an area of a probe array. Furthermore, no cited prior art provides an improvement to the Andrevski design that would be capable of hybridization of a small fluid volume over an area of a probe array using the flexible diaphragm. Therefore, independent claims 45 and 91 are patentable over the cited prior art.

The Examiner also rejected claims 74 and 99 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,168,948 in view of Andrevski et al. and Southgate et al. Applicants respectfully disagree with this rejection if again applied to the amended claims. The above-cited claims or the cited prior art does not describe a low volume hybridization device that would be capable of hybridization of a small fluid volume over an area of a probe array.

Therefore, all pending claims are now in condition for allowance and such action is respectfully solicited. Should there be any outstanding issue left, the Examiner is respectfully invited to call the undersigned at the telephone number below.

Please charge all PTO fees and apply all credits to the Deposit Account No. 01-0431.

Respectfully submitted,

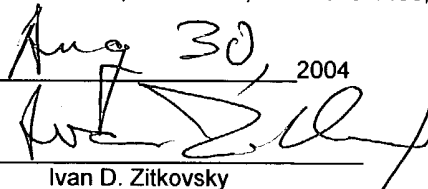


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